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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/619,520	RICHTER ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *1-12 and 16-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/13/06*.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5)☐ Notice of Informal Patent Application

6)☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 9/13/06, is acknowledged.

2. Claims 1-25 are pending.

3. Claims 1-12 and 16-25 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention. Regarding the rejoinder of claims 2-4, 10-12 and 16-17, until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims is maintained.

Upon reconsideration the Examiner has extended the species search to cover SEQ ID NO:2.

4. Claims13-15 are under under examination as they read on an adsorber column comprising a matrix and a ligand, wherein the ligand has specificity for fibrin and/or firbrinogen and the species of SEQ ID NO:1 and SEQ ID NO:2.

5. Applicant's IDS, filed 9/13/06, is acknowledged, however, the International Search Report (reference No. I) was crossed out but the references listed thereon had been considered.

6. The following new ground of rejections are necessitated by the amendment submitted 9/13/06.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 13-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrase "useful individually or as one of a pair or more of absorber columns for influencing the microcirculation of a mammal" claimed in claim 13, lines 10-11 represents a departure from the specification and the claims as originally filed.

Applicant's amendment filed 9/13/06 points to the specification one page 6, linwa 12-24, page 7, lines 27-28 and figure 1 for support for the newly added limitations "useful individually or as one of a pair or more of absorber columns for influencing the microcirculation of a mammal" as claimed in claim 13. However, the specification does not provide a clear support for such limitation. The instant claims now recite limitations which were not clearly disclosed in the specification and recited in the claims as originally filed.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 13 is indefinite in the recitation of "influencing" in the claim is ambiguous and unclear and the metes and bounds of the claimed "influencing" is not defined. It is unclear what is the effect of adsorber column on microcirculation.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 13-15 are rejected under 35 U.S.C. 103(a) as being obvious over Kuyas (1995b) *et al* (Thrombosis and Haemostasis, 1995, vol. 54, No. 1, pp. 40-40) in view of U.S. Pat. NO. 5,079,155.

Kuyas et al (1995) teach an adsorber column containing Gly-Pro-Arg-Pro-Sepharose, wherein the Gly-Pro-Arg-Pro (GPRP) is the ligand and Sepharose is the matrix (see the entire abstract). Kuyas et al teaches GPRP-Sepharose affinity chromatograpy is a fast and reproducible method and ideal for the isolation of fibrinogen from small a mounts of plasma. It is superior to any available method for the isolation of abnormal fibrinogens provided the c-terminal binding site is intact (see the entire abstract).

The claimed invention differs from the Kuyas et al (1990) teachings only by the recitation of a polylysine or a ε-amino acapronic acid spacer in claim 13 and 14.

The `155 patent teaches that the addition of a spacer group can result in even higher retention of biological activity of ligand or binder. Spacers suitable for this purpose can be derived from polylysine and 6-aminocaproic acid (col., 8, lines 30-37 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add a polylysine or ε-amino acapronic acid taught by the `155 patent to the peptide ligand taught by the Kuyas et al to increase the retention of the biological activity of the ligand.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the addition of a spacer group, such as polylysine and amino acapronic acid, can result in even higher retention of biological activity of ligand or binder as taught by the `155 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. Claims 13-14 are rejected under 35 U.S.C. 103(a) as being obvious over Kuyas (1990a) *et al* in view of U.S. Pat. NO. 5,079,155.

Kuyas *et al* teach the Gly-Pro-Arg-Pro-Lys-Fractogel (acrylic glass) adsorber column containing a matrix (Fractogel) and a ligand (Gly-Pro-Arg-Pro-Lys) claimed SEQ ID NO:2, wherein the Gly-Pro-Arg-Pro-Lys ligand has a specificity for fibrin and/or fibrinogen (see abstract and page 440, col., 1 paragraphs 2-4 in particular).

The claimed invention differs from the Kuyas et al (1990) teachings only by the recitation of a polylysine spacer in claim 13 and 14.

The `155 patent teaches that the addition of a spacer group can result in even higher retention of biological activity of ligand or binder. Spacers suitable for this purpose can be derived from polylysine and 6-aminocaproic acid (col., 8, lines 30-37 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add a polylysine taught by the `155 patent to the peptide ligand taught by the Kuyas et al to increase the retention of the biological activity of the ligand.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the addition of a spacer group, such as polylysine, can result in even higher retention of biological activity of ligand or binder as taught by the `155 patent.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. Claim 15 is rejected under 35 U.S.C. 103(a) as being obvious over Kuyas (1990a) *et al* in view of U.S. Pat. NO. 5,079,155 as applied to claims 13-14 above, and further in view of Kuyas (1995b) *et al.*

The teachings of Kuyas et al (1990) and the `155 patent have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation that the matrix is a carbohydrate matrix in claim 15.

However, Kuyas et al (1995b) teach an adsorber column containing Gly-Pro-Arg-Pro-Sepharose, wherein the Gly-Pro-Arg-Pro (GPRP) is the ligand and Sepharose is the matrix (see the entire abstract). Kuyas et al teaches GPRP-Sepharose affinity chromatograpy is a fast and reproducible method and ideal for the isolation of fibrinogen from small a mounts of plasma. It is superior to any available method for the isolation of abnormal fibrinogens provided the c-terminal binding site is intact (see the entire abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the Fractogel (acrylic glass) taught by the Kuyas (1990) with the Sepharose matrix taught by Kuyas (1995b).

One of ordinary skill in the art at the time the invention was made would have been motivated to do so to have the peptide distant enough form the gel matrix a further amino acid, lysine, is included in the peptide as a spacer as taught by Kuyas (1990a) *et al.*

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. In view of the amendment filed on 9/13/06, only the following rejections are remained.

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuyas (1990a) *et al* (IDS ref. NO. 2).

Kuyas *et al* teach the Gly-Pro-Arg-Pro-Lys-Fractogel (acrylic glass) adsorber column containing a matrix (Fractogel) and a ligand (Gly-Pro-Arg-Pro-Lys) claimed SEQ ID NO:2, wherein the Gly-Pro-Arg-Pro-Lys ligand has a specificity for fibrin and/or fibrinogen (see abstract and page 440, col., 1 paragraphs 2-4 in particular).

The reference teachings anticipate the claimed invention.

Applicant's arguments, filed 9/13/06, have been fully considered, but have not been found convincing.

Applicant argues that that Kuyas et al 1990, do not disclose the features recited in the claims. Applicant further argues that Kuyas et al 1990 appears be limited to the isolation and purification of fibrin or fibrinogen in pooled plasma, while the instant claims recite the surprising finding that with the help of adsorber columns, effective in vitro treatment of a patient's or a mammal's blood (i.e., an ex vivo treatment) influencing blood rheology in the patient or mammal can be realized.

Examiner position is the amended claims recite the same products and the intended uses do not carry patentable weight per se and the claims read on the active or essential ingredients of the Gly-Pro-Arg-Pro-Lys-Fractogel (acrylic glass) adsorber column.

Applicant further submits that Kuyas et al 1990 appears to be limited to an adsorber column containing a Fractogel matrix (a synthetic methacrylate based polymeric resin), while the instant claims recite that the matrix comprises a material selected from glass, carbohydrates and polyamides.

However, Fractogel matrix, a synthetic methacrylate based polymeric resin, is also called acrylic glass. Since the specification does not provide any limiting definition of the word "glass", the prior art's Farctoget matrix, i.e., acrylic glass, would appear to be encompassed by the broadest reasonable definition of a "glass".

18. Claims 13-15 are rejected under 35 U.S.C. 103(a) as being obvious over Kuyase (1990a) *et al* in view of Kuyas (1995b) *et al.*

The teachings of Kuyas (a) *et al* reference have been discussed, supra. Kuyas (1990a) *et al* further teaches that human fibrinogen has a strong affinity for fibrin. Therefore, fibrin immobilized on Sepharose is used to isolate fibrinogen from human plasma by affinity chromatography. Kuyas *et al* further teach that the terapeptide GlyProArgPro, containing the N-terminal sequence of the α-chain of fibrin being exposed upon the action of thrombin on fibrinogen, competitively inhibits the fibrin polymerization. It also binds to fibrinogen. In addition the N-terminal amino acid sequence GlyProArg is involved in the inhibition of the fibrin polymeriazation by binding to the complementary binding site of an other fibrin(ogen) molecule (see *Introduction* on page 439 in particular). Lastly Kuyas et al teach that the addition of a second proline enhances the affinity of the peptide Gly ProArgPro for fibrinogen almost tenfold.

Further, to have the peptide distant enough form the gel matrix a further amino acid, lysine, was included in the peptide as a spacer (see page 443, 1st col., last full paragraph in particular).

The claimed invention differs from the Kuyase (a) *et al* reference teachings only by the recitation that the matrix is a carbohydrate matrix in claim 15.

However, Kuyas et al (1995b) teach an adsorber column containing Gly-Pro-Arg-Pro-Sepharose, wherein the Gly-Pro-Arg-Pro (GPRP) is the ligand and Sepharose is the matrix (see the entire abstract). Kuyas et al teaches GPRP-Sepharose affinity chromatograpy is a fast and reproducible method and ideal for the isolation of fibrinogen from small a mounts of plasma. It is superior to any available method for the isolation of abnormal fibrinogens provided the c-terminal binding site is intact (see the entire abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the peptide GlyProArgPro taught by Kuyas (1995b) et al with the pentapeptide GlyProArgProLys taught by Kuyas (1990a) *et al.*

One of ordinary skill in the art at the time the invention was made would have been motivated to do so to have the peptide distant enough form the gel matrix a further amino acid, lysine, is included in the peptide as a spacer as taught by Kuyas (1990a) *et al.*

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments, filed 9/13/06, have been fully considered, but have not been found convincing.

Applicant argues that the amended claim 13 recites a feature "influencing the microcirculation" that is not found in the combined reference teachings.

Examiner position is the intended uses do not carry patentable weight per se and the claims read on the active or essential ingredients of the resultant Gly-Pro-Arg-Pro-Lys-carbohydrate adsorber column.

Applicant also argues that Kuyas et al 1995 teach an adsorber column containing Gly-Pro-Arg-Pro-sepharose for use in affinity chromatograph, while the amended claims recite X to be polylysine ....

However, SEQ ID NO: 2 has no X and therefore, the argument is irrelevant to SEQ ID NO:2.

19. No claim is allowed.

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

September 22, 2006

Maher Haddad

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